Deceased donor transplantation in the elderly—are we creating false hope?

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Abstract

Background. Increasing numbers of older patients are developing established renal failure and considering kidney transplant as a renal replacement therapy (RRT) option. The probability of older patients actually receiving a deceased donor kidney transplant is unclear, preventing informed choice about pursuing the option of transplantation. We sought to analyse our RRT population to determine the probability of receiving a deceased donor kidney transplant in patients commencing RRT categorized by age and for whom there was no suitable living kidney donor.

Methods. Patients commencing dialysis in our centre between 1992 and 2009 were identified. Time to listing on the deceased donor transplant waiting list and time to first deceased donor transplant were determined by Kaplan–Meier analysis for patients, categorized by age, with censoring at the date of first living donor kidney transplant, death or last dialysis.

Results. One-thousand-five-hundred-and-thirteen patients were categorized into groups by age in years [1: <35 (n = 134), 2: 35–49.9 (n = 207), 3: 50–64.9 (n = 415), 4: >65–74.9 (n = 438) and 5: ≥75 (n = 319)]. The probability of being listed for deceased donor transplant within 1 year of commencing RRT was 75, 54, 27, 4 and 0.8% in Groups 1–5, respectively. If listed, the probability of receiving a deceased donor transplant within 5 years of starting RRT was 81, 48, 26, 8 and 0% in Groups 1–5, respectively. In Groups 1–4, 93% (n = 63), 87% (n = 65), 76% (n = 45) and 100% (n = 7) of the patients, respectively, who received a deceased donor transplant were alive and off dialysis 1 year after transplant. The reason patients who were listed did not receive a transplant was usually death on the waiting list.

Conclusions. The likelihood of being listed for transplant falls with increasing age at the time of starting RRT. Even for patients listed for transplant, the probability of older patients actually receiving a transplant is much lower than for younger patients, with only 8% of listed patients aged 65–74.9 years being transplanted within 5 years. This is partly the result of death on the waiting list but may also be related to organ allocation policies. Assessment for possible deceased donor transplantation involves a considerable investment in time and effort for the patient, as well as in health care resources, and a patient's decision whether to proceed with assessment should be informed by the kind of information we have produced. As there may be regional and national variations in practice, each centre should generate such data for use locally.

Keywords: deceased donor; dialysis; elderly; kidney transplant; transplant assessment

Introduction

Kidney transplantation improves life expectancy and quality of life in patients with end-stage renal disease (ESRD) [1,2]. Assuming a patient is felt to be fit enough for transplantation, this statement holds true regardless of age with the caveat that the survival advantage in those >70 years is only evident from ~2 years following the transplant operation [1–5]. Deceased donor transplantation seems to be cost effective in older recipients provided a donor is found within 2 years of a recipient being listed on the deceased donor waiting list and live donor transplantation is economically sound regardless of age and time on the waiting list [1,6].

There are many in whom transplantation is not a viable option and although advancing age is not a contraindication per se, older patients are more likely to have or to develop an absolute or a combination of relative contraindications to transplantation which mean the risks of the operation and the use of immunosuppressive drugs might outweigh any benefit [7,8].

As the general population ages, increasing numbers of patients aged >65 years are developing ESRD and considering renal replacement therapy (RRT) including transplant-
In the UK in 2008, the median age of patients starting RRT was 64.1 years; almost 50% of patients commencing RRT are aged ≥65 years [9]. Age is an important determinant of access to the deceased donor waiting list and patients aged >65 years have a lower probability of being referred and listed even in the absence of an absolute contraindication to transplantation when compared with their younger counterparts [10–12]. The explanation for this is likely to be multifactorial and include patient preference, the presence of comorbid conditions which make transplantation less feasible option, physician opinion and organ allocation policies.

Pre-transplant assessment, undertaken to assess suitability for transplant, uses considerable healthcare resources and can be time consuming. There is a paucity of information about the probability of older patients actually receiving a deceased donor kidney transplant to enable them to make an informed decision as to whether to pursue the option of being worked up for deceased donor transplant listing, if there is no living donor option. Our local perception was that elderly patients undergo detailed assessment and counselling before being listed for deceased donor transplant but rarely actually receive a kidney. We were concerned that we were falsely raising hopes in these elderly patients. We therefore sought to analyse our own RRT population in order to determine the probability of receiving a deceased donor kidney transplant in patients commencing RRT categorized by age and for whom there was no suitable living kidney donor.

Materials and methods

All patients commencing either peritoneal or haemodialysis in our centre and its associated satellite units between January 1992 and December 2008 were identified from the electronic patient record. Patients who wish to consider kidney transplant and are considered by their nephrologist to be potentially fit for transplant are seen in a transplant assessment clinic. Our assessment of suitability for transplantation is consistent with the UK guidelines [13]. Briefly, this involves exclusion of contraindications and cardiac assessment if there is a history of cardiovascular disease or diabetes or if a patient is aged ≥50 years. Initial cardiac investigations involve a 12 lead electrocardiogram, treadmill exercise testing and echocardiography. Further assessment with cardiac MRI scan and coronary angiography is dependent upon clinical judgement [14].

Case notes and the electronic patient record were used to record the dates of first transplant assessment visit, activation on the deceased donor transplant waiting list, first transplant operation (live or deceased) and death/lost to follow up. Statistical analysis was performed using the SPSS statistics package (version 15, SPSS Inc.). Deceased donor kidney transplants were allocated via the UK national allocation scheme (see discussion). Time to listing on the deceased donor transplant waiting list and to first deceased donor transplant were determined by Kaplan–Meier analysis for patients, categorized by age, with censoring at the date of first living donor kidney transplant, death or when lost to follow up. The actuarial probability of receiving a deceased donor transplant was calculated from survival tables generated by Kaplan–Meier analysis.

For the recipient, transplant work up for a live or deceased donor kidney transplant is virtually identical. Suitable patients are, therefore, often listed for deceased donor transplant even if there is a live donor option. If live donation goes ahead, the patient is deactivated from the deceased donor waiting list. Under some circumstances, a patient may receive a renal transplant before commencing regular dialysis: a pre-emptive transplant. This is much more likely with a live donor transplant but can occur with a deceased donor. In our analysis, patients receiving a pre-emptive live donor transplant were excluded (n = 41).

Results

One-thousand-six-hundred-and-ninety-two patients commenced dialysis during the period of interest. One-hundred-and-seventy-nine of these patients were excluded because they recovered renal function, received a kidney and pancreas transplant or received a pre-emptive live donor transplant. The study population, of 1513 patients, was categorized into five groups by age in years; 1: 18–34.9 (n = 134), 2: 35–49.9 (n = 207), 3: 50–64.9 (n = 415), 4: 65–74.9 (n = 438) and 5: ≥75 (n = 319). This is illustrated in Figure 1. During the follow-up period, 19% (n = 285) of the whole cohort received a kidney transplant of which 21% (n = 60) were from live donors (Figure 2). The probability of being listed for a deceased donor transplant was 75, 54, 27, 4 and 0.8% in Groups 1–5, respectively (Table 1). If listed, the probability of receiving a deceased donor transplant within 5 years of starting RRT was 81, 48, 26, 8 and 0% in Groups 1–5, respectively (Figure 3). Those in the younger age categories were significantly more likely to receive a transplant and to receive it earlier than their older counterparts; after a median wait of 1.32 years in Group 1 compared with 9.8 years in Group 4 (P < 0.001). In Groups 1–4, 93% (n = 63), 87% (n = 65), 76% (n = 45) and 100% (n = 7) of patients, respectively, who received a deceased donor transplant were alive and off dialysis 1 year following transplant. The reason for patients who were listed but did not receive a transplant was usually death on the waiting list (Table 2). Of those currently active on the transplant waiting list, the median waiting time within Groups 1–4, respectively, is 2.4, 2.13, 2.6 and 2.5 years. In Group 5, of the three patients listed for transplant, one died 2.8 years after listing and the other two had been waiting for 6 months and 2.4 years at the time of analysis. In Groups 1–5, 50, 51, 66, 81 and 82% of the patients, respectively, not listed for transplant died within 24 months of commencing RRT.

Discussion

Our data demonstrate that the likelihood of being referred for and of receiving a deceased donor kidney transplant falls with advancing age at the time of commencing RRT. What is surprising is the very low probability of
receiving a deceased donor kidney transplant in elderly patients listed for deceased donor transplant (<4% in the first 5 years after transplant listing in patients aged >65 years). This has not been shown before and other units should be encouraged to perform a similar analysis in their own population. We speculate that, if presented with these data, some elderly transplant candidates would be more keen to pursue living transplant offers from spouses or adult children, and some would elect not to pursue transplantation at all.

In our patient population, within each age category, a large proportion of those who were not listed for transplant died within 24 months of commencing RRT, suggesting that the transplant assessment process correctly identified patients likely to have been too frail to undergo transplantation and unlikely to have survived to reap the benefits of transplantation compared with dialysis. Any potential transplant recipient must have a reasonable probability of surviving both on the waiting list and after the transplant operation. Naturally, this probability falls with increasing age.

The difference in the probability of patients who were listed for deceased donor transplant actually receiving a transplant according to recipient age was striking: 81% for the youngest patients and 4% for those aged between 65 and 74.9 years. Death on the waiting list and suspension from the waiting list after development of new morbidities are both more common with advancing age and may provide some explanation. In addition, the UK deceased donor kidney allocation policy tends to favour younger recipients in common with other organ allocation organizations internationally. Deceased donor kidneys for transplant are a scarce resource and the allocation of them is therefore very challenging: the aim is to balance equity of access with the best use of the resource. Generally, there is consensus that to strike this balance and to get the best long-term benefit from the kidneys, there must be a degree of weighting towards transplanting kidneys from younger donors to younger recipients. How to achieve this optimally remains a topic of debate.

To allocate a new deceased donor kidney, the UK allocation scheme awards points based on a number of factors to each potential recipient. Briefly, each time a donor kidney becomes available, all patients on the deceased donor waiting list with the same blood group are allocated a score which is based upon time on the waiting list, human leucocyte antigen (HLA) matching with the donor kidney and age combined (points increase with better HLA match and lower age), difference in donor and recipient age (points reduce as age gap increases) and geographical location of recipient and donor. Paediatric patients (patients aged ≤18 years) are prioritized and if a patient is active on the transplant waiting list before their 18th birthday, they retain paediatric status until they are completely removed from the list [15]. Transplants with no HLA A, B and DR mismatches are also prioritized. The allocation scheme changed in April 2006 in
an attempt to allocate kidneys more fairly by reducing the emphasis on HLA matching and increasing the emphasis on minimizing waiting time. It has been shown that with this new UK allocation scheme, the chance of receiving a kidney for older patients is slightly reduced compared with similarly HLA-matched younger recipients and this relates to the smaller number of older deceased donors [15,16].

Within Europe, The Eurotransplant Senior Programme (ESP) was created to allow more efficient use of kidneys from elderly donors and to facilitate transplantation in elderly patients. ESP allocates kidneys to recipients aged ≥65 years from donors and aged ≥65 years regardless of HLA matching. Between 1999 and 2003, this resulted in a 55% increase in recipients aged ≥65 years receiving a kidney and an increase in the number of elderly donor kidneys [17]. Recipients allocated a kidney via ESP rather than via the traditional HLA-driven Eurotransplant Kidney Allocation System have shorter waiting times and less delayed graft function [18]. Data suggest that there is no significant difference in graft or patient survival between those allocated a kidney from an elderly donor via ESP and those receiving a similar kidney from EKTAS [17,19].

The UK population is aging resulting in increased numbers of elderly patients commencing RRT and increased numbers of donor kidneys aged ≥65 years [20]. The ESP model is perhaps one way of allocating donor organs more effectively while encouraging consideration of transplantation in older patients.

Assessment for possible deceased donor transplantation involves considerable investment for both the patient and

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Table 2. Outcome of dialysis patients (1992–2008) on the basis of whether they were or were not on the kidney transplant waiting list

<table>
<thead>
<tr>
<th>Age category (years), n</th>
<th>1 (18–34.9)</th>
<th>2 (35–49.9)</th>
<th>3 (50–64.9)</th>
<th>4 (65–74.9)</th>
<th>5 (≥75)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>134</td>
<td>207</td>
<td>415</td>
<td>438</td>
<td>319</td>
</tr>
<tr>
<td>Listed for transplant</td>
<td>114 (85%)</td>
<td>152 (73%)</td>
<td>162 (39%)</td>
<td>31 (7%)</td>
<td>3 (1%)</td>
</tr>
<tr>
<td>Transplanted (live/deceased)</td>
<td>105 (92%)</td>
<td>95 (63%)</td>
<td>75 (46%)</td>
<td>10 (32%)</td>
<td>0</td>
</tr>
<tr>
<td>Listed but not transplanted</td>
<td>9 (8%)</td>
<td>57 (37%)</td>
<td>77 (54%)</td>
<td>21 (68%)</td>
<td>3 (1%)</td>
</tr>
<tr>
<td>Deceased on waiting list</td>
<td>2 (2%)</td>
<td>27 (18%)</td>
<td>42 (26%)</td>
<td>7 (23%)</td>
<td>1 (33%)</td>
</tr>
<tr>
<td>Not listed</td>
<td>20 (15%)</td>
<td>55 (27%)</td>
<td>253 (61%)</td>
<td>407 (93%)</td>
<td>316 (99%)</td>
</tr>
<tr>
<td>Assessed but not listed^4</td>
<td>6 (30%)</td>
<td>25 (45%)</td>
<td>65 (26%)</td>
<td>17 (4%)</td>
<td>0</td>
</tr>
<tr>
<td>Not listed and now deceased</td>
<td>10 (50%)</td>
<td>34 (62%)</td>
<td>207 (82%)</td>
<td>344 (85%)</td>
<td>260 (82%)</td>
</tr>
<tr>
<td>Alive and not listed</td>
<td>6 (30%)</td>
<td>17 (30%)</td>
<td>34 (13%)</td>
<td>52 (13%)</td>
<td>39 (12%)</td>
</tr>
<tr>
<td>Lost to follow up</td>
<td>4 (20%)</td>
<td>4 (7%)</td>
<td>12 (5%)</td>
<td>11 (3%)</td>
<td>17 (6%)</td>
</tr>
</tbody>
</table>

^4Put forward for formal assessment but following this not deemed fit enough to be put onto the waiting list.
the health care system. Age is not a contraindication but the survival and economic advantages take longer to materialize with advancing recipient age. Live donor transplantation is advantageous earlier and should be pursued if it is an option. Traditionally, there have been barriers both from patients themselves and from health care professionals in transplanting from a younger donor to a significantly older recipient—‘transplanting up a generation’.

Our data have some potential limitations. They come from a single centre which means that the approach to transplant assessment was relatively consistent. However, it also means that our findings may not be applicable to other populations, although it is likely that the results will be similar to the rest of the UK since the allocation scheme is national. The retrospective nature of the data collection may not be as robust as a prospective study although the data were mainly collected from the prospectively maintained recorded electronic patient record. We included patients from both before and after the change in the UK organ allocation policy but most of the study period was before April 2006 and it therefore seems unlikely that this has led to significant bias. As stated above, the probability of elderly patients receiving a kidney has probably reduced slightly since the new allocation scheme was introduced.

Any future activity that can reduce the overall waiting list for deceased donor kidneys may improve the access for all age groups to deceased donor transplant and recent drives in the UK towards increasing live donor transplant and transplants from non-heart-beating donors may eventually start to reduce the waiting list. While this might give grounds for optimism that the probability of older recipients receiving a transplant kidney might improve, recent trends suggest that the number of available deceased donor kidneys will not keep up with the number of patients listed for transplant.

Conclusions

Age should not deter patients or physicians from considering deceased donor transplantation. However, with advancing age, if there is no live donor option, then the probability of receiving a deceased donor transplant falls significantly within the current UK organ allocation scheme. Our analysis provides clinicians and patients with new information to allow RRT planning in the older patient with advanced chronic kidney disease who has no live kidney donor option or is reluctant to consider live donation offers such as spousal donation or donation up a generation. We hope that our analysis will encourage other centres to produce similar data to inform their own practice.

Conflict of interest statement. None declared.

(See related article by de Fijter. Counselling the elderly between hope and reality. Nephrol Dial Transplant 2011; 26: 2078–2081.)

References


Received for publication: 20.10.10; Accepted in revised form: 20.12.10